

CLAIMS

1. A short interfering RNA (siRNA) molecule that down regulates expression of a p65 subunit of NF-kappa-B gene by RNA interference, said siRNA molecule comprising a sense region and an antisense region and wherein said antisense
5 region comprises a sequence complementary to an RNA sequence encoding the p65 subunit of NF-kappa-B and the sense region comprises a sequence complementary to the antisense region, **characterized** in that said antisense region comprises a sequence substantially complementary to a sequence chosen among SEQ ID NOs. 1, 2, 3 and 4 and wherein said antisense region comprises
10 a sequence chosen among SEQ ID NOs. 5, 6, and 8 or substantially homologous sequences thereof.
2. The siRNA molecule of claim 1, wherein said sense region comprises a sequence chosen among SEQ ID NOs 9, 10, and 12 or substantially homologous sequences thereof.
- 15 3. The siRNA molecule of claim 1, wherein said sense region and antisense region are covalently connected via a linker molecule.
4. The siRNA molecule of claim 1, wherein said linker molecule is a polynucleotide linker.
5. The siRNA molecule of claim 1, wherein said linker molecule is a non-
20 nucleotide linker.
6. The siRNA molecule of claim 1, wherein said sense region comprises the sequence of SEQ ID NO. 9 and said antisense region comprises the sequence of SEQ ID NO. 5.
7. The siRNA molecule of claim 1, wherein said sense region comprises the
25 sequence of SEQ ID NO. 10 and said antisense region comprises a sequence of SEQ ID NO. 6.

8. The siRNA molecule of claim 1, wherein said sense region comprises the sequence of SEQ ID NO. 12 and said antisense region comprises the sequence of SEQ ID NO. 8.
9. The siRNA molecule of any one of claims 1 – 8, wherein said sense region
5 comprises a 3'-terminal overhang and said antisense region comprises a 3'-terminal overhang.
- 10 The siRNA molecule of claim 9, wherein said 3'-terminal overhangs each comprising 1 to 5 natural or modified nucleotides.
11. The siRNA molecule of claim 9, wherein said antisense region 3'-terminal
10 nucleotide overhang is complementary to RNA encoding p65 subunit of NF-kappa-B.
12. The siRNA molecule of claim 1, wherein said sense region comprises one or more 2'-O-methyl modified pyrimidine nucleotides.
13. The siRNA molecule of claim 1, wherein said sense strand comprises a
15 terminal cap moiety at the 5'-end, 3'-end, or both 5' and 3' ends of said sense region.
14. The siRNA molecule of claim 1, wherein said antisense strand comprises one or more 2'-deoxy-2'-fluoro modified pyrimidine nucleotides.
15. The siRNA molecule of claim 1, wherein said antisense and/or sense strand
20 comprises between one and up to and including five phosphorothioate internucleotide linkages at the 3' end of said antisense region.
16. The siRNA molecule of claim 1, wherein said antisense and/or sense strand comprises between one and up to and including five phosphorothioate internucleotide linkages at the 5' end of said antisense region.

17. The siRNA molecule of claim 9, wherein said 3'-terminal nucleotide overhangs comprise ribonucleotides that are chemically modified at a nucleic acid sugar, base, or backbone.
18. The siRNA molecule of claim 9, wherein said 3'-terminal nucleotide
5 overhangs comprise deoxyribonucleotides that are chemically modified at a nucleic acid sugar, base, or backbone.
19. The siRNA molecule of claim 9, wherein said 3'-terminal nucleotide overhangs comprise one or more universal base ribonucleotides.
20. The siRNA molecule of claim 9, wherein said 3'-terminal nucleotide
10 overhangs comprise one or more acyclic nucleotides.
21. The siRNA molecule of claim 9, wherein said 3'-terminal nucleotide overhangs comprise nucleotides or non-nucleotides
22. An expression vector comprising a nucleic acid sequence encoding at least one siRNA molecule of claim 1 in a manner that allows expression of the nucleic
15 acid molecule.
23. A mammalian cell comprising the expression vector of claim 22.
24. The mammalian cell of claim 23, wherein said mammalian cell is a human cell.
25. The expression vector of claim 22, wherein said siRNA molecule comprises a
20 sense region and an antisense region and wherein said antisense region comprises sequence complementary to an RNA sequence encoding p65 subunit of NF-kappa-B and the sense region comprises sequence complementary to the antisense region.
26. The expression vector of claim 22, wherein said siRNA molecule comprises
25 two distinct strands having complementarity sense and antisense regions.

27. The expression vector of claim 22, wherein said siRNA molecule comprises a single strand having complementary sense and antisense regions.

28. A method of preventing, treating or alleviating NF-kappa-B dependent conditions in an individual, which comprises administering a therapeutically effective amount and in a suitable pharmacological carrier, a siRNA compound of claim 1, so that expression of the p65 subunit of NF-kappa-B is suppressed, thereby suppressing NF-kappa-B dependent processes.

29. The method of claim 28, wherein the NF-kappa-B dependent condition is selected from cancer, cardiac disorders, ischaemia, allergic/inflammatory diseases and conditions, including but not limited to asthma, allergic rhinitis, atopic dermatitis, psoriasis, rheumatoid arthritis, ulcerative proctitis, ulcerative colitis, Crohn's disease, septic shock, and other diseases or conditions that are NF-kappa-B dependent.

30. A method of preventing, treating or alleviating NF-kappa-B dependent conditions in an individual, which comprises the extraction of cells, tissue or entire organs from said individual; contacting the said cells, tissue or entire organs with a siRNA compound of claim 1, so that expression of the p65 subunit of NF-kappa-B is suppressed, thereby suppressing NF-kappa-B dependent processes; and reintroducing the same.

31. The method of claim 30, wherein said method is used as a step in a treatment involving one of transplantation, graft, or implantation.
